

Implementation of CDISC Standards at Nycomed

PhUSE SDE Eschborn, 06-MAY-2009

Agenda



- **Background**
- **Clinical data warehouse FACT**
- **CDISC implementation**
- **Current Nycomed CDISC standards**
- **Conclusions and outlook**

Partnering – Together for medicines that matter



Nycomed is actively seeking partnerships

- Co-development from early research on
- In-licensing for marketing by Nycomed
- Out-licensing where Nycomed is not present



The R&D Operating Model – contribution of Data Science



In-house

- **State-of-the-art statistical capabilities**
 - for statistical input into protocol and drug development plans
- **Maintenance of standards**
 - Data acquisition
 - **Data integration**
 - Data quality
- **Ensure availability of integrated clinical trial data for pooled analyses**
(Data Warehouse Development, operation and maintenance)

Outsourced

- **Data cleaning process and database set-up outsourced** (to a large proportion)
Flexible data management capacities available for in-house processing as well as for supervision of Data Management CROs
- **Study specific statistical reporting and generation of analysis data bases**
outsourced with flexible resources for CRO supervision.

Heterogeneous Data Sources

- **CRO databases**
 - standardised SDTM domains based on Nycomed requirements
 - ADaM datasets
- Data from **in-licensing** partners
 - what-ever-they-have structures
- **Legacy** data from two prior companies
 - what-ever-we-have structures

Agenda



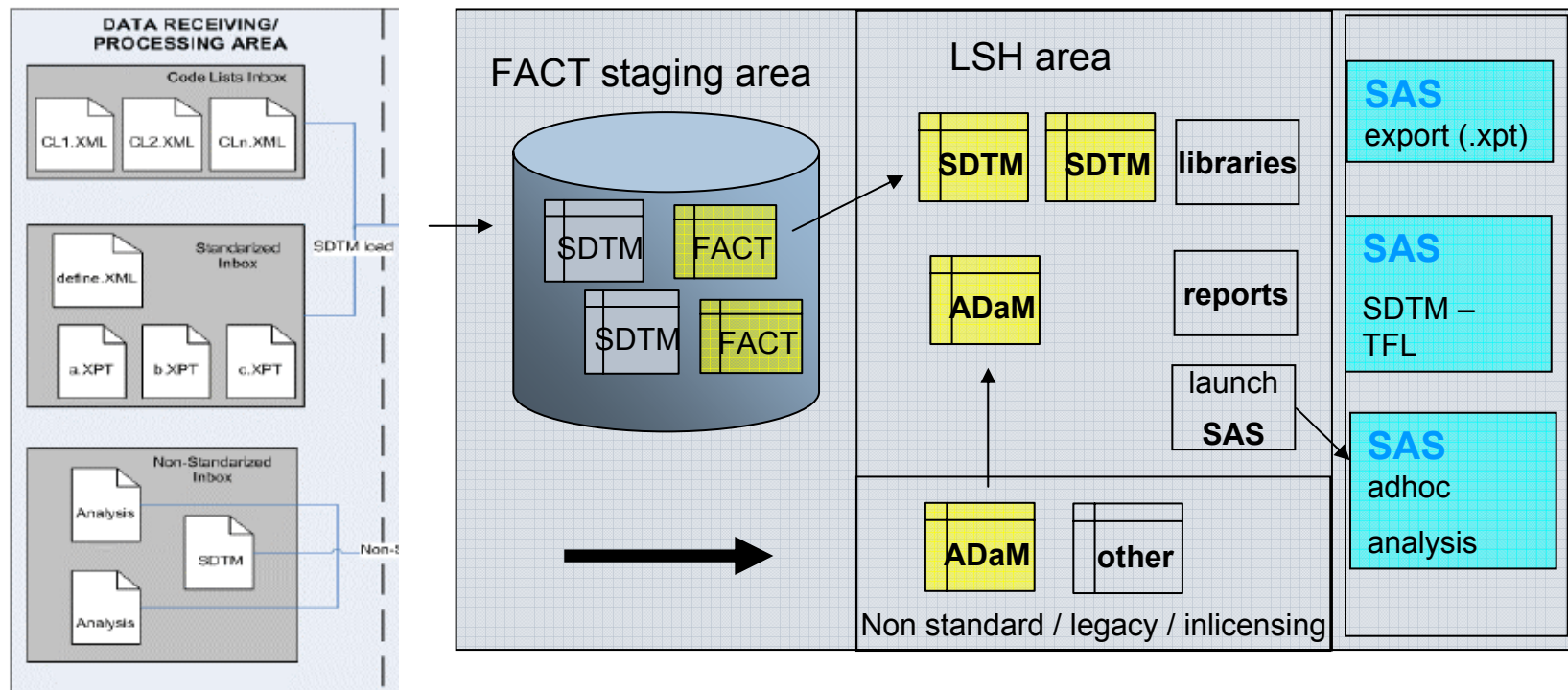
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FACT objectives

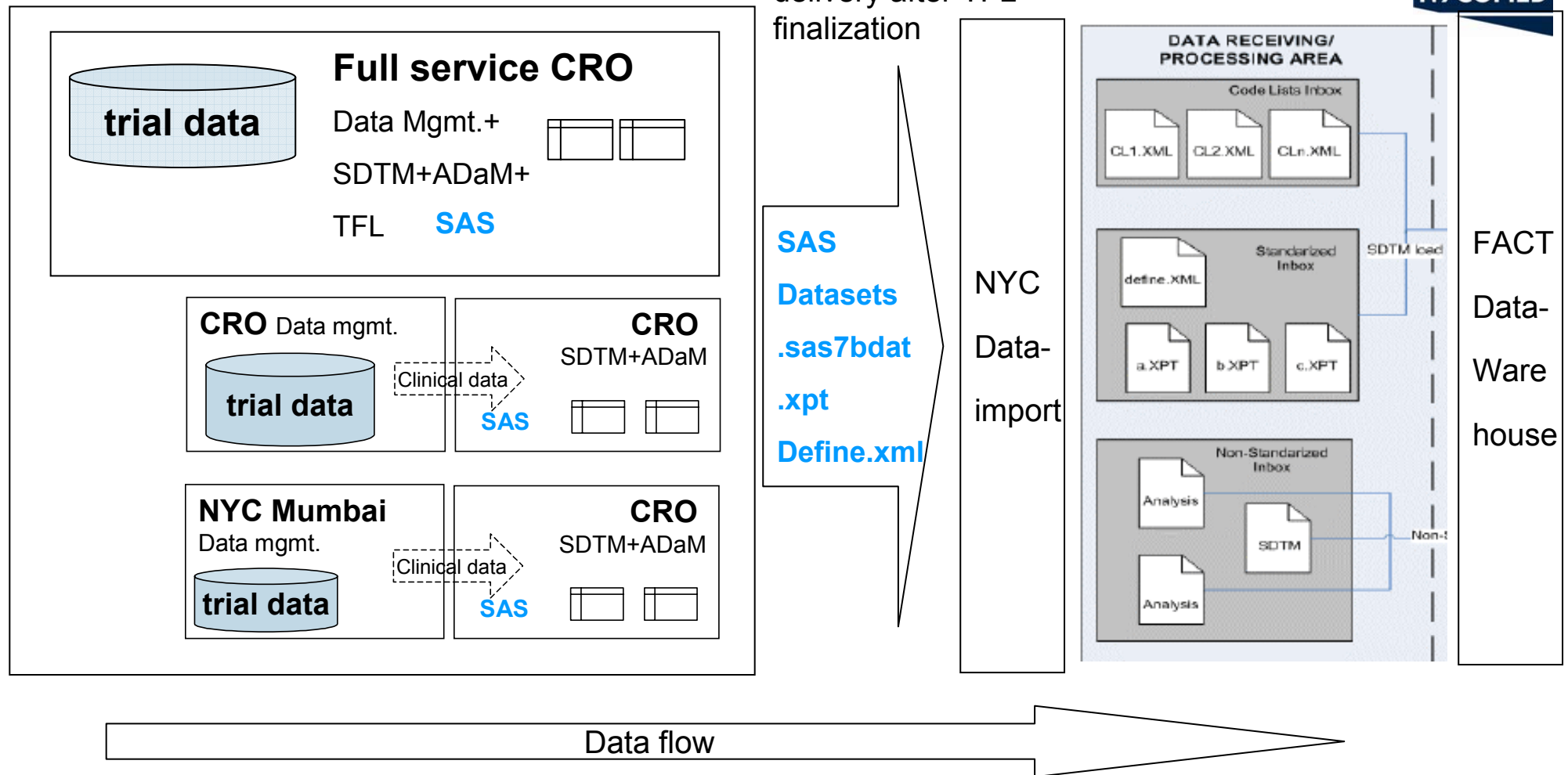


- Ability to **protect** and **explore** one of the main assets of our company: Clinical Trial Data
- **Optimise** procedures for **exchange** of clean clinical trial data with external and internal partners
- Ensure data **integrity**
- **Acquire data** of partners in licensing projects secure and quickly
- Provide a platform for storage of **legacy** data
- Data **availability** for all data-related questions
- Ensure **compliance** with regulations (21 CFR part 11, ICH E9)

Clinical data warehouse FACT



Data flow and data processing

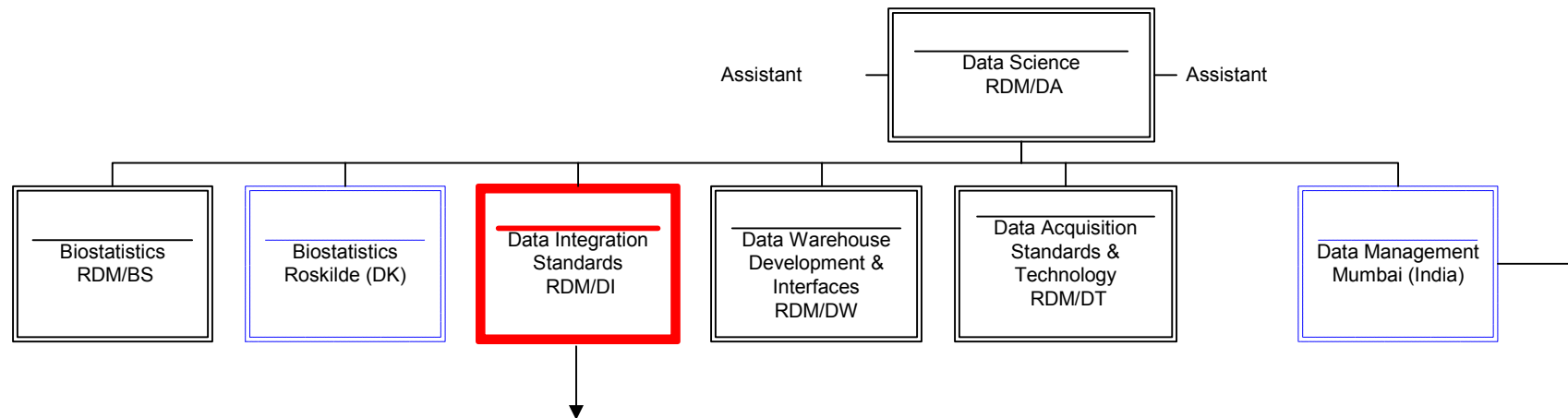


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Global CDISC initiative



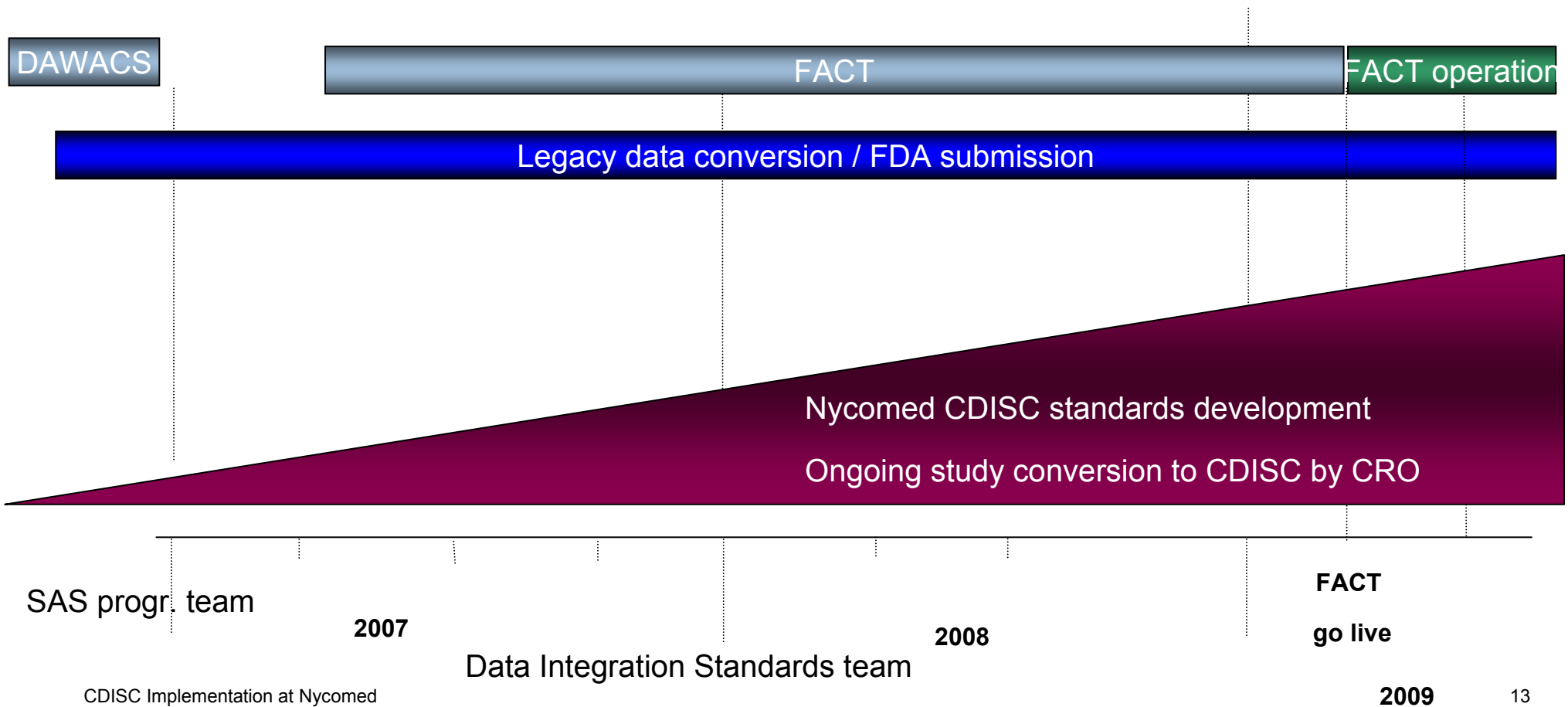
1. Building of a CDISC **SDTM** and **ADaM** standards competence centre which coordinates all activities related to these standards within Nycomed R&D and between Nycomed and partners
2. Development of
 - Global in-house standards / processes / QC concept
 - CRO interfaces / deliverables and processes
3. Development of a dataset repository (windows file system, physical import and export)
4. Contribution to the FACT project / data warehouse operation and maintenance

Dpt. Data Integration Standards – the FACT / CDISC team



Role	No of individuals	Tasks / responsibilities
CDISC coordinator	1	Scope, process definition, strategy, submission
DIM - Data Integration Manager - Study setup - Data import/export - Integration/codelists - QC - Maintenance	2	- SDTM ongoing and legacy - SDTM Phase I / PK
	1	- ADaM / define.xml / ODM - SAS Server, batch jobs, export - SAS QC SDTM- TFL compare - SAS toolkit
	1	- Data import and export - LiveLink administration / user accounts - codelists

CDISC and FACT development at Nycomed



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„How we work with CROs“ – CDISC standards

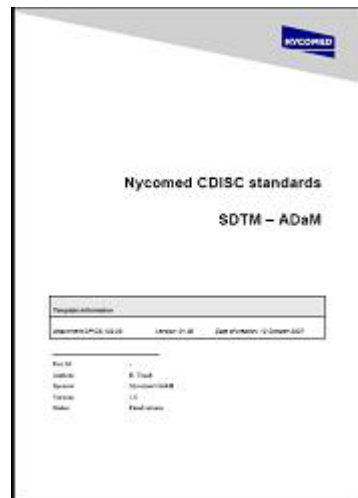
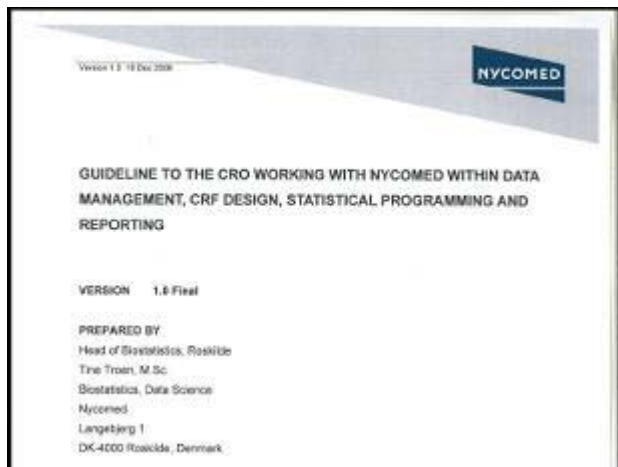


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20	Final remarks
21	Appendices
21.1	Nycomed Data Science responsible persons per function for this project
21.2	How to work with Nycomed templates.....
21.3	Template for CRFs - Not yet available.....
21.4	DM documents/templates (DHP, DVP, DHR).....
21.5	Template for CRF
21.6	General requirements on CDISC, SDTM and ADaMs
21.7	SOP responsibilities within the CRO and within Nycomed
21.8	Mandarin template for tables, figures and listings documents
21.9	Template for tables, figures and listings (standard mock-ups) - Not yet available.....
21.10	Template for BDRM documentation - Not yet available.....
21.11	Format for data transfers

Processes



- CDISC deliverables, requirements and processes are generally described in a **project plan** including QC plans.
- The SDTM mapping is based on a SDTM annotated CRF (**aCRF**), (non-EDC studies)
- SDTM and ADaM **specification** (URS)
 - Contain all information about domains, variables, computation rules, etc
 - Serve as a basis to create the define.xml file
- Communication:
 - The discussion of content issues is generally done by means of **'issue logs'**
 - **Emails** are generally restricted to organisational or administrative messages.
- **SAS programming**: external provider are required to do all programming of SDTMs, ADaM and TFLs in SAS. (SAS program validation acc. to provider SOPs).

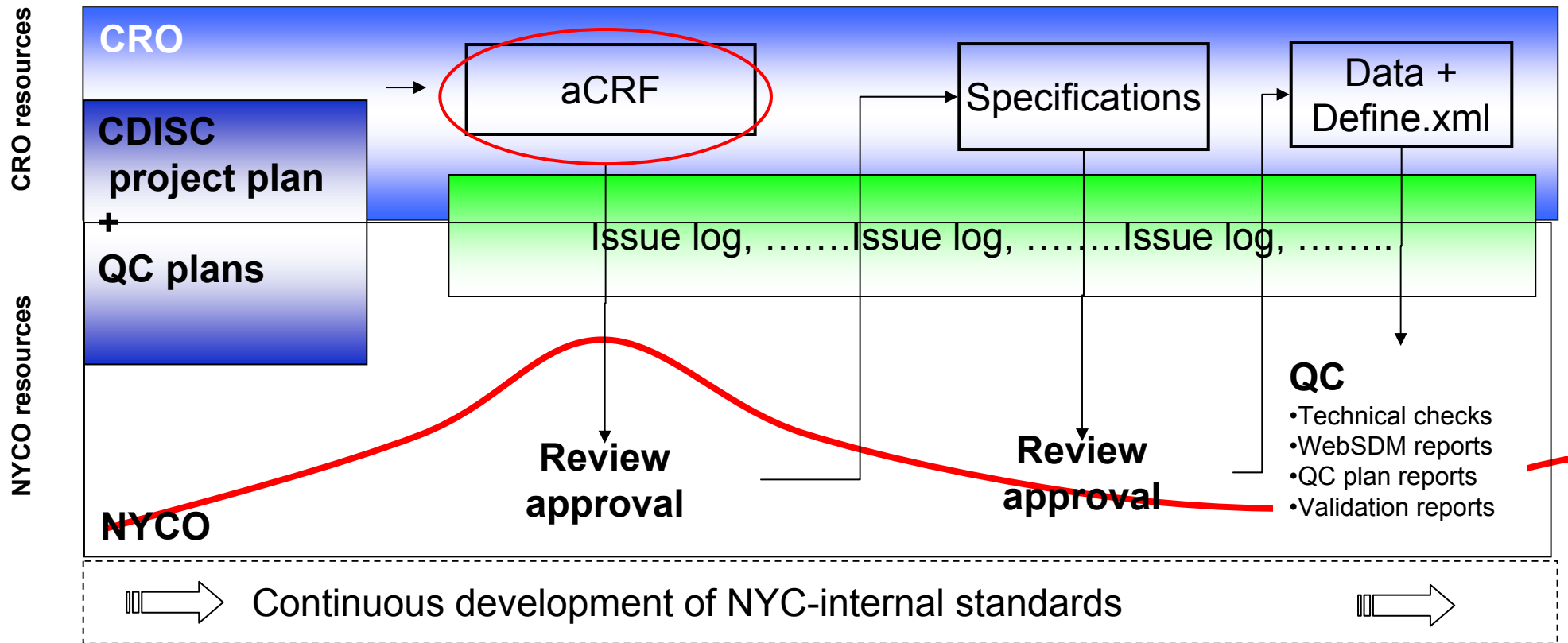
SDTM ADaM mapping



Study Data Tabulation Model
Implementation Guide:
Human Clinical Trials
Prepared by the
CDISC Submission Data Standards Team

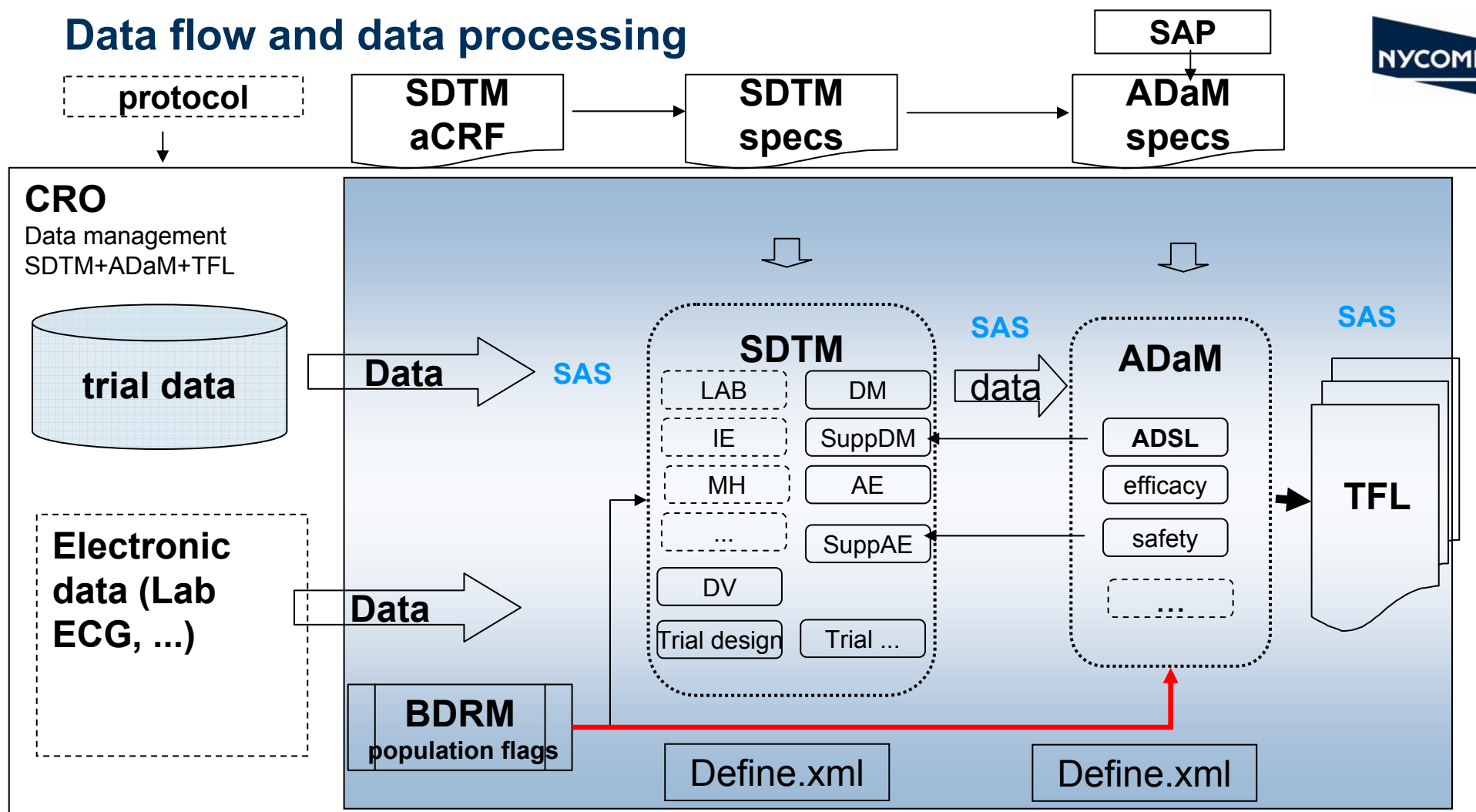


Analysis Data Model: Version 2.0
Prepared by the
CDISC Analysis Dataset Modeling Team
(ADaM)



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Data flow and data processing



Define.xml

- **Guidelines and rules**

- CRT-DDS V 1.0 (define.pdf will not be accepted)
- CDISC 'Metadata Submission Guidelines, Appendix to the SDTM IG V3.1.1'
- CDISC ODM V 1.2 standard (machine-readability)
- Naming conventions according to ICH eCTD

- **Separate** define files for SDTM and ADaM domains;

- **Consistency checks:**

- Number of datasets and variables included
- Dataset names and labels
- Variable names, labels, data type (expressed in ODM terminology)
- Order of variables within a dataset
- Consistency of values of variables regulated by controlled terminology
- FACT requirements

ADaM define



Analysis Datasets for Study BY217_CP-069

Dataset	Description	Structure	Purpose	Keys	Location	Documentation
ADSL	Subject Level	One record per subject	Analysis	STUDYID, USUBJID	adsl.xpt	See program: adsl.pdf
ADAE	Adverse Events	One record per subject per treatment per adverse event term per start date/time	Analysis	STUDYID, USUBJID, TRTA, AETERM, AESTDTM	adae.xpt	See program: adae.pdf
ADEG	ECG	One record per subject per parameter per analysis visit per analysis timepoint	Analysis	STUDYID, USUBJID, PARAM, AVISIT, ATMVISIT	adeg.xpt	See program: adeg.pdf
ADEGS	ECG (derived)	One record per subject per treatment per parameter	Analysis	STUDYID, USUBJID, TRTA, PARAM	adegs.xpt	

Go to the top of the [define.xml](#)

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Subject Level Dataset (ADSL)

Variable	Label	Type	Length/Format	Controlled Terminology	Source/Computational Method
STUDYID	Study Identifier	text	12		DM.STUDYID
USUBJID	Unique Subject Identifier	text	21		DM.USUBJID

Analysis Results Metadata (Detail) for Study BY217_CP-069

Analysis	Table 13.2.1: Summary of Subject Characteristics
Description	Frequency distribution of Gender and Race. Descriptive statistics of Age at Day 1, Weight at Screening, Height at Screening and BMI.
Reason	
Data References	Subject Level (ADSL) [Safety Flag = 'Y']
Documentation	slsum.pdf , See CSR 6.4

Go to the [Analysis Results Metadata Summary](#)

Analysis	Table 13.6.3: Summary of TESS Adverse Events
Description	Number of subjects with TESS AEs and associated TESS AEs. Number of TESS AEs and associated TESS AEs. Both by Treatment Group and Intensity. Number of withdrawals due to TESS AEs, number of serious TESS AEs and number of deaths by Treatment Group.
Reason	pre-specified in protocol
Data References	Adverse Events (ADAE) [TRTEMFL = 'Y' for TESS AEs, AEREL = 'LIKELY' for associated AEs]
Documentation	aesum.pdf , See CSP 9.4 and CSR 9.1

Go to the [Analysis Results Metadata Summary](#)

Analysis	Table 13.9.1: Summary of OT Results by Treatment Group - Day 1
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QC



- **Quality control of SDTM, ADaM datasets is based on**

- QC check plan
- **WebSDM edit checks** of SDTM datasets enhanced by study/project specific checks
- Nycomed relies on compliance to good clinical - and good programming practice.

CRO

- **Internal QC**

- Checksum / xpt files
- Schema conformity to ODM 1.2
- Consistency checks SDTM / ADaM (such as primary keys, variable naming and completeness, Null values)
- Final SDTM contents check after FACT upload (SDTM-TFL)

NYC

Deliverables summary

- **SDTM aCRF**
 - Annotation of variables and variable values
 - Top level bookmarks
- **CDISC SDTM datasets (.xpt/.sas7bdat) + define.xml**
- **CDISC ADaM datasets (.xpt/.sas7bdat) + define.xml**
 - SAS programs for ADaMs (.pdf/.sas)
 - SAS programs for TFLs (.pdf /.sas)
- **Final specification documents**
 - SDTM
 - ADaM
- **Quality Checks (QC)**
 - QC plans
 - QC reports (in particular WebSDM edit check reports)
 - Validation reports

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Lessons learned



Contracting external partners for CDISC data conversion tasks is more than just telling the partner to refer to the current CDISC SDTM/ADaM and define.xml standards

- Important
 - CROs experience and
 - Stable CDISC standard SDTM V 1.1 / IG V 3.1.1
- Main task
 - Development of internal standards
 - CDISC knowledge / training of employees
- In general, the CDISC standards are of high value and in particular the results published from the SDTM/ADaM pilot provided excellent examples



Thank you

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